AMENDMENTS TO THE SPECIFICATION

Please replace the title at page 1, line 1 with the following title:

--Protein Variants of Naturally Occurring Allergens--

Please replace the paragraph beginning at page 18, line 28 with the following paragraph:

--Figure 21: Amino acid alignment of rMal d 1 ~~Mal d 1~~ (2620) and Bet v 1.2801. Position no. above sequences refers to Mal d 1 (accession no. AJ488060). Positions no. below sequences refers to Bet v 1 (accession no. Z80104). Black background shows positions in the polypeptide sequences having identical amino acid residues. Grey background shows positions in the polypeptide sequences having homologous amino acid residues. Amino acid positions that in example 3 are targeted for introduction of secondary mutations are indicated with triple bars on black background and amino acid positions for introduction of primary mutations are indicated with black arrows.--

Please replace the paragraphs beginning at page 20, line 12 with the following paragraphs:

--Figure 25: Composition in secondary structure elements of rMal d 1 ~~Mal d 1~~ (2620), rMal d 1 ~~Mal d 1~~ (2762), rMal d 1 ~~Mal d 1~~ (2781) and Bet v 1.2801, obtained by the deconvolution of their CD spectra. The deconvolution sets of rMal d 1 ~~Mal d 1~~ (2762), rMal d 1 ~~Mal d 1~~ (2781) and Bet v 1.2801 fall within the acceptance boundaries determined for the reference protein, rMal d 1 ~~Mal d 1~~ (2620) (±15%), and therefore these four proteins may be considered to be structurally similar with respect to secondary structure.--

Figure 26: Biacore experiment. Binding of the monoclonal antibody BV16 to rBet v 1.2801, non-mutated rMal d 1 ~~Mal d 1~~ (2620) and mutated rMal d 1 (2781). No binding was observed with non-mutated rMal d 1 (2620). rBet v 1.2801 and mutated rMal d 1 (2781) are both bound by BV16.--

Please replace the paragraph starting at page 30, line 12 with the following paragraph:

--In an embodiment, where rMal d 1 ~~Mal d 1~~ (2620) (database accession number: AJ488060) is the Bet v 1 scaffold protein, a protein variant comprises at least two primary mutations selected from the group consisting of: (E12V, E12I, E12M, E12L), P16A, (H40S, H40T), I43N, L44I, D47N, G65K, K70R, (E76H, E76R, E76K, Q76H), S107T, G108P, +109D, S110G, E129A, K152L, (P154S, P154T), P155S and optionally one or more secondary mutations are selected from the group consisting of: N28X, preferably N28T, K32X, preferably K32Q, E45S, E96X, +159X. In this context, as well as in the following examples, the first letter and number corresponds to the original amino acid code in a particular amino acid position. The following letter is the amino acid that can be substituted with the original amino acid. Parenthesis means that there are a number of different options when choosing to mutate in a given amino acid position. One of these can be chosen.--

Please replace the paragraphs starting at page 31, line 5 with the following paragraphs:

--In another specific embodiment, a protein variant of a Mal d 1 protein variant (rMal d 1 (2781)) comprises the sequence defined in SEQ ID NO 2:

GVYTYENEYTSEIPPPRLFKAFVLDADNLIPKIAPQAIKHAENIEGNGGPGTIKKITFGEGSQY
KYVKHRIDSVDHANYSYAYTLIEGDALTDTIEKVSYETKLVASGSGSIIKSISHYHTKGDVEI
MEEHVKAGKEKAHGLFKLIESYLKDHPDAYN,

said variant comprising the following primary mutations: I43N, L44I, D47N, G65K, K70R, Q76H. The rMal d 1 (2781) variant is an example of a protein variant according to the present invention that has increased Bet v 1 specific IgE reactivity in comparison with the "native" rMal d 1 ~~Mal d 1~~ 2620. This is illustrated in detail in the Examples.

In yet another specific embodiment, a protein variant of a Mal d 1 protein variant (rMal d 1 (2762)) comprises the sequence as defined in SEQ ID NO 3:

GVYTYENEYTSVIPPARLFKAFVLDADNLIPKIAPQAIKHAEILEGDGGPGTIKKITFGEGSQ
YGYVKHKIDSVDEANYSYAYTLIEGDALTDTIEKVSYETKLVATPDGGSIIKSISHYHTKGD
VEIMEEHVKAGKEKAHGLFKLIESYLLDHSDAYN,

said variant comprising the following mutations: E12V, P16A, K152L, P155S, S107T, G108P, +109D, S110G. "+" means in this context ~~connection~~ insertion of an amino acid at the indicated position. The rMal d 1 (2762) variant is an example of a protein variant according to the present invention that has increased Bet v 1 specific IgE reactivity in comparison with the "native" rMal d 1 ~~Mal d 1~~. This is illustrated in detail in the Examples.--

Please replace the paragraph beginning at page 32, line 6 with the following paragraph:

--According to a fifth embodiment a protein variant of the present invention is a protein variant wherein Dau c 1 (~~datsabase~~ database accession number: T14325) is a scaffold protein of Bet v 1. According to this embodiment, a protein variant of Dau c 1 comprises at least two primary mutations selected from the group consisting of: (S12V, S12L, S12I, S12M), S14P, E16A, P105A, A107P, (A148S, A148T), (I151L, I151V, I151M), (N153H, N153K, N153R), (+154S, +154T), (+155D, +155E), +156A, (+157Y, +157F), (+158N, +158Q), (K39S, K39T), (K44E, K44D), (V52I, V52M, V52L), (I54K, I54R, I54H), (T64K, T64R, T64H), (T65Y, T65F, T65W), (T67K, T67R, T67H), D86E, L91G, (G92D, G92E) and optionally one or more secondary mutations are selected from the group consisting of: K32X, E42X, E59X, R69X, E95X, K122X, E8X, T10X, D25X, ~~K32X,~~ D46X, ~~E59X, E95X,~~ D108X~~, K122X~~.--

Please replace the paragraph beginning at page 36, line 24 with the following paragraph:

--In a ~~thirteen's~~ thirteenth preferred embodiment of the present invention, the naturally occurring allergen is a fungal protein.--

Please replace the paragraph starting at page 49, line 9 with the following paragraph:

--All Mal d 1 mutants were generated as follows. First (I), each single mutation (or several mutations if located closely together in the DNA sequence) were introduced into DNA sequences coding for rMal d 1 ~~Mal d 1~~ (2620) (accession number: AJ488060) using sense and anti-sense mutation-specific oligonucleotide primers accommodating each mutation(s) along with sense and anti-sense oligonucleotide primers accommodating either upstream or downstream neighbour mutations or the N-terminus/C-terminus of Mal d 1, respectively as schematically illustrated in

Figure 1 (I). Secondly, PCR products from PCR reactions (I) were purified by agarose gel electrophoresis and PCR gel purification, mixed and used as templates for an additional PCR reaction (II) with oligonucleotide primers accommodating the N-terminus and C-terminus of Mal d 1 as schematically illustrated in Figure 1 (II). The PCR products were purified by gel electrophoresis and PCR gel purification followed by ethanol precipitation, cut with restriction enzymes (Sac / EcoRI) or (SacI / XbaI), and ligated directionally into pMAL-c restricted with the same enzymes.--

Please replace the paragraph starting at page 61, line 10 with the following paragraph:

--This example is based on modification of rMal d 1 ~~Mal d 1~~ (2620) (accession no. AJ488060). Amino acid residue position numbering in the following refers to AJ488060 as shown in figure 21. The example is based on the introduction of one or more of the following secondary mutations: E8X, N28X, K32X, E96X and amino acid insertion +X159 (X being any amino acid residue). In one preferable embodiment of the invention one or more of the introduced amino acid residues (X) may be amino acid residues that are homologous to Bet v 1 specific residues for each of the individually corresponding positions. Homologous amino acid residues are: E=D, V=L=I=M, S=T, Y=F=W, K=R=H, N=Q, where (=) indicates that two or more amino acid residues are homologous. The following mutations are suggested: E8D, N28Q, K32R or K32H, E96D. The example further includes the introduction of one or more of the following primary mutations where introduced mutations are residues that are identical or homologous to corresponding amino acid residues in any known isoforms of Bet v 1. The following mutations are suggested: E12V or E12I or E12M or E12L, H40S or H40T, E76H orE76R or E76K, E129A, P154S or P154T. Protein sequences with mutated amino acid residues are shown in figure 21.--

Please replace the paragraph starting at page 63, line 25 with the following paragraph:

--According to Fig. 25, the deconvolution sets of rMal d 1 ~~Mal d 1~~ (2762), rMal d 1 ~~Mal d 1~~ (2781) and Bet v 1.2801 fall within the acceptance boundaries determined for the reference protein, rMal d 1 ~~Mal d 1~~ (2620) (±15%), and therefore these proteins may be considered to be structurally (secondary structure) similar.--